EXHIBIT

“C”

UNITED STATES DISTRICT COURT

SOUTHERN DISTRICT OF WEST VIRGINIA

CHARLESTON DIVISION

IN RE: ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION	**Master File No. 2:12-MD-02327** **MDL 2327** **JOSEPH R. GOODWIN** **U.S. DISTRICT JUDGE**
THIS DOCUMENT RELATES TO: *Wave 4 Cases*	

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Expert Report on TVT-O

Background and Qualifications:

I am currently a practicing physician, licensed in the state of Pennsylvania. I obtained my medical degree from the University of Montreal Canada in 1988. I then went on to complete a residency in obstetrics and gynecology in 1993. In the following year, I did a one year minimally invasive laparoscopic and hysteroscopic fellowship in Clermont-Ferrand, France. I have obtained certification from the Canadian Medical Council, the Quebec Board of Specialties, the Royal College of Physicians and Surgeons of Canada and American Board of Obstetrics and Gynecology. In June 2013, the first year the certification exam was conducted, I became board certified in Female Pelvic Medicine and Reconstructive Surgery.

In 1994, I began my career in a group setting, tertiary center and university teaching hospital at Notre-Dame Hospital in Montreal Canada, where I practiced until August 1997. Through a recruiter, I found my way to York, Pennsylvania, joining a solo practitioner until he passed away in 1998. Since then I have been in a mostly solo practice. I have been teaching residents in obstetrics and gynecology since 1994. Early in my career, I devoted my efforts mostly to gynecology with a special interest in urogynecology, focusing on pelvic pain, pelvic prolapse and incontinence. Initially I included general obstetrics in my practice, which I stopped in 2008. I have performed most surgeries through a minimally invasive approach. By my training and experience, I am familiar with laparotomy (open), laparoscopic and robotic techniques, as well as vaginal approaches for prolapse and incontinence surgeries.

I have witnessed and participated in the evolution of our understanding of pelvic organ prolapse and incontinence. During my fellowship, the surgical treatment of pelvic floor prolapse and incontinence was innovative and the use of minimally invasive technique was very different than the traditional repairs I learned during my residency training. Since 1994, I have performed open, but mostly laparoscopic sacrocolpopexies, intra-peritonal colpopexies, para-vaginal repairs and Burch urethropexies. I also performed autologous fascial slings during my residency. I have also performed thousands of vaginal surgeries with and without synthetic mesh for pelvic organ prolapse, including but not limited to colpocleisis, traditional anterior and posterior repairs, sacrospinous ligament fixation, uterosacral ligament colpopexies. I have also performed hundreds of anti-incontinence procedures including retropubic and transobturator midurethral slings, including TVT and TVT-O.

I have also developed expertise in the management of chronic pelvic pain, voiding and defecation dysfunction, as well as the management of postoperative complications to include correction and repair of mesh involved surgeries as well as treatment of patients' symptoms.

Throughout the world, not just in the USA, there has been a need for better understanding and better repair techniques in our quest to help patients, keeping in mind decreased morbidity and mortality. Vaginal surgeries performed 30 years ago for the treatment of urinary incontinence had excessive failure rates. Open laparotomy techniques for the correction of urinary incontinence, including the MMK, Burch, Pubovaginal slings and others, are associated with increased morbidity associated with wound infection, adhesions and injury to abdominal and pelvic organs, bleeding, increased pain and a significantly longer recovery time. Often women would be discharged with catheters for days, weeks or more. It's no wonder that our mothers and grandmothers suffered in silence. With our aging population, as well as the ever increasing rate of morbid obesity, even the laparoscopic or robotic approach are placing patients at increased risks compared to a vaginal approach. It is this with this understanding that the need to improve the durability of repairs that has led to the notion of augmentation or reinforcement of the already weakened pelvic and periurethral support in a minimally invasive fashion.

I started using the TVT device in 2002, and eventually began using the TVT-O. I have experience with other outside-in technique as well. I am familiar with their training and the information provided to surgeons, including IFU's, surgical videos, Surgical Technique Guide and Surgeon's Monograph, and other training materials. I am aware of the FDA public health notices of 2008 and 2011, the FDA's 2013 statement on midurethral slings, as well as the reclassifications of 2016 and 2017. As a urogynecologist, it is my professional obligation to keep myself up-to-date with the current literature, including peer reviewed applications regarding synthetic mesh.

In preparation of this report, I have considered the published medical literature available along with the opinions, recommendations and positions of statement from various medical societies and governmental agencies. In forming my opinions, I also considered my own training and experience. All opinions offered are held to a reasonable degree of medical certainty. I reserve the right to amend my opinions pending reception of additional literature, records, transcripts, or expert reports.

Pelvic Organ Prolapse:

Issues of pelvic prolapse and incontinence are increasing in prevalence in the United States and around the world as women are living longer. It is estimated from the Women's Health Initiative and various other studies that the prevalence of incontinence varies between 25 and 50%, and the prevalence of prolapse although based on varying definitions of prolapse varies between 15 and

41%. Both can coexist and the incidence increases with age. It is estimated that 11% of women have a lifetime incidence of undergoing pelvic organ prolapse surgical repair. Market data showed that in 2010, 260,000 women underwent surgery for stress incontinence, and 80% were performed transvaginally with synthetic midurethral slings. Approximately 300,000 women underwent surgery for pelvic floor prolapse either as in or outpatient, and approximately one third used mesh; and of those three quarters were performed using a vaginal approach. These figures are estimated to increase by nearly 50% over the next 40 years (Dieter, 2015). Risk factors for pelvic organ prolapse are well known, and include advancing age, race, menopause, connective tissue disorders, obesity, vaginal parity, and smoking. Studies have shown that concurrent pelvic organ prolapse surgery at the time of hysterectomy and pelvic organ prolapse as an indication for hysterectomy are significant risk factors for pelvic organ prolapse later in life (Lykee 2015). In a study evaluating data from 154,882 women who underwent hysterectomy for benign indications, recurrence of pelvic prolapse most often was associated the initial indication of prolapse for the hysterectomy.

Although pelvic floor prolapse is not an immediate life threatening condition, it can affect lower and upper urinary tract function, bowel and defecation, pressure or discomfort, and sexuality. Overall, symptomatic pelvic organ prolapse can substantially affect quality of life. Most women will not be aware of their prolapse until it descends to the hymen and beyond, or until the development of new symptoms. Pelvic pressure, discomfort with activities and the feeling of bulging within the vagina are frequently reported as the prolapse worsens. Some patients become uncomfortable with intercourse, not only due to a negative body image, but depending on the compartment prolapse and associated midline fascial defect there can be forceful pressure directly onto the bladder or the rectum, increased forceful displacement of the prolapsed vaginal apex or uterus within the pelvis, thus causing intercourse to become physically uncomfortable and even painful. The cervical or vaginal mucosa, once descended below the hymen, comes in contact with the patient's underwear or pad. This can lead to irritation, ulceration, bleeding, abnormal discharge and chronic infection of the vaginal mucosa. Women have been known to put Vaseline, Crisco, olive oil, diaper creams and various over the counter creams and lotions as these symptoms progress.

Anterior wall prolapse is often associated apical prolapse symptoms, which can include a feeling of pelvic pressure, frequency, urgency and incontinence. As the prolapse worsens, there may be an associated "kinking" of the urethra. These women may experience symptoms of hesitancy and difficulty urinating, sometimes needing to reduce the prolapse digitally to assist voiding. As the anterior vaginal wall and bladder continue to fall well below the hymen, bulging discomfort associated with sitting or activities may progress, along with issues of incomplete bladder emptying, recurrent urinary tract infections, and an increased incidence of kidney infections. If left untreated, retention, hydronephrosis and kidney damage can occur.

Posterior wall prolapse symptoms include pressure or bulging symptoms with accumulation of stools within the protrusion, difficulty with defecation leading to excessive straining or assistance with splinting or fingering to empty out the rectal ampulla, as well as fecal smearing and incontinence. Conversely, functional disorders such as chronic constipation or dyssynergic/obstructed defecation (abnormal non-relaxation or spasms of the levator ani muscles during defecation, may coexist with a posterior defect but are often mistakenly attributed to a visible rectocele or perineocele. Surgical correction in these patients will often lead to good anatomical success without treating the underlying cause and will not meet patient's expectations.

In antiquity, various forms of pessaries and belts have been described through the ages, until surgical options have been become available in the last two centuries. Non-surgical options include pelvic floor exercises such as kegels. Although some studies show improvement in urinary stress incontinence with some protection in cases of stage I prolapse, none of these studies conclude that pelvic floor exercises have any benefits to treat organ descent below the hymeneal ring.

The debate for the optimal route of pelvic prolapse surgery has been going on for almost 100 years. Until the advent of laparoscopic and robotic surgeries for prolapse in the last 25 years, the risk of additional morbidity via laparotomy incisions has meant that the vaginal approach should be encouraged whenever possible. Unfortunately, some report the persistence, recurrence or de-novo prolapse to be as high as 60% within 1 year (Whiteside, 2004). The optimal approach for the repair of pelvic organ prolapse is still not known. A surgeon must consider the type of prolapse, their own surgical skills and expertise as well as patient factors including obesity, previous abdominal and pelvic surgeries and other medical co-morbidities, when deciding the route of surgery.

Obliterative surgery such as colpocleisis and colpectomy are the least invasive of all prolapse surgery. There are reports of failures, stress incontinence, infection with pyometria. Of course, these obliterative procedures should be considered on a select group of patients and reserved for women who are certain they will never want to be vaginally sexually active in the future.

Vaginal prolapse surgery to maintain a functional vagina without graft augmentation essentially involves trying to reattach or correct a defect using the patient's own, already weakened tissue. The quality and strength of a patient's vaginal mucosa, ligaments and fibromuscular layers will influence the resilience and longevity of the repair, as these are the same tissues that have failed and contributed to the prolapse in the first place.

The anterior vaginal wall is the most frequent location of both primary and recurrent prolapse. The failure rates for these traditional repairs have been cause for concern as repeat surgeries in a previously scarred vagina can cause even more overall morbidity. When one considers that a woman who undergoes pelvic floor surgery at age fifty might live into her mid-eighties, most studies do not currently reflect the true long term effects of our procedures.

Abdominal and vaginal paravaginal repairs have been around for decades. In the last 25 years, surgeons have introduced the laparoscopic approach. They are intended to recreate the level 2 support at the Arcus Tendineus Fascia Pelvis (ATFP), which restores the mid vaginal physiological axis. The risks of these procedures include the above and hemorrhage from the pelvic vasculature, nerve damage due to the extensive dissection throughout the fibromuscular layer, as well as ureteral and bladder injuries. The vaginal paravaginal repair was recently quoted as a technique with "complication rates seem unacceptably high" (Brubaker, 2010).

Traditional posterior repair involves midline plication of the fibromuscular layer using interrupted delayed absorbable sutures, resection of excess vaginal mucosa an in most cased it is associated with a perineoplasty in which the diameter of the introitus is reduced. The occurrence of post-operative sexual dysfunction is well known and has been cause for concern after rectocele repairs especially if concomitant urethropexy of Burch (Weber, 2000). Even native tissue repair, with or without associated hysterectomy, can lead to pelvic pain, dyspareunia (18-38%), issues with incontinence and all other general risks associated with surgery and anesthesia. Symptoms of splinting, straining, incomplete evacuation and obstructive defecation present before surgery, may or may not improve after the surgical repair (Paraiso, 2001). Symptoms such as straining decreased from 74% pre-operatively to 23% post-operatively, and incomplete evacuation and obstructive defecation persisted in 19% and 14% of patients respectively. Splinting was found to still be present in 23% (compared to 56%) and was associated with a longer history of splinting before the surgical repair.

Vaginal native tissue procedures that suspend the apex includes sacrospinous ligament fixation, which deviates the axis of the vagina posteriorly and laterally – usually to the right side. It is associated with a higher recurrence of anterior vaginal prolapse (28.8%) and stress urinary incontinence (Morgan, 2007). Iliococcygeal fascia repair is similar, but results in a more posterior displacement of the vagina associated with an increased risk of stress urinary incontinence and recurrence of prolapse of the anterior vagina. The 2015 Up to date report on surgical repair of vaginal apical prolapse describes a dyspareunia rate of 36% for the sacrospinous ligament fixation procedure (Kenton, 2015).

McCall/modified McCall culdoplasty and High Uterosacral Ligament suspension involve either a hysterectomy or usually opening the vaginal cuff with intraperitoneal access. Recurrence, or new

prolapse can occur, as well as dyspareunia (22% for the modified technique are documented) only 2 years was 64.5% for the uterosacral ligament and 63.1% for the sacrospinous ligament suspension. Notably 16.5% of patients experienced a serious adverse event.

In the management of apical prolapse, abdominal sacrocolpopexy has long been regarded as having the most durable long term results, but with increased morbidity and longer convalescence. A comprehensive review of abdominal sacrocolpopexy (Nygaard, 2004) reported intra-operative complications involving perforations of the bladder (3.1%), bowel (1.6%) and ureteral injury (1%). The incidence of hemorrhage and transfusions was 4.4%. Also, post-operative complications included wound herniation requiring repair (5%), transient ileus (3.6%) and bowel obstruction requiring surgery (1.2%). Cases of necrosing fasciitis, lumbar diskitis and osteomyelitis have also been documented, with devastating consequences. In addition, painful intercourse has been reported in 16% (Kenton, 2015) and de-novo dyspareunia 14.5% (Handa, 2007). Mesh erosion rates were reported to be 10.5% at 7 years in the E-CARE trial (Nygaard 2013). More recently reports of de novo unprovoked vaginal pain in the absence of mesh erosion have surfaced (Buechel, 2016). Urinary incontinence is a well-known occurrence after sacrocolpopexy, even in previously continent women. Over 45% of women will suffer from de novo urinary incontinence if a prophylactic anti incontinence is not performed concomitantly. It is now suggested proceed with a prophylactic urethropexy or sling procedure in addition to the saccrocolpopexy. Despite this additional surgery, over 20% of women will still have problems with urinary incontinence (Brubaker-CARE trial, 2006). As noted in the most recent Cochrane review of apical prolapse surgery comparing abdominal to laparoscopic or robotic, the data reflects mostly post hysterectomy patients and most importantly, “not all women are suitable for sacrocolpopexy” (Maher-2016).

Pelvic Pain:

Chronic pelvic pain including dyspareunia are problems that can affect 8 to 22% of women at some point in their life (Latthe, 2006). In the United States, it is estimated that chronic pain syndromes affect 34% of all women (Brennan-2007). Crombie-1998 reported a survey of 5000 patients seen in chronic pain centers found that 34.2% had pain from degenerative disease and 22.8% of patients complained of chronic pain after surgery, making it the second most common complaint. Other U.S. based studies have shown a high rate of chronic pelvic pain, persistent dyspareunia, sexual dysfunction, and IBS amongst the general population of women (Mathias, 1996; Jamieson, 1996, Laumann, 2004).

Pelvic pain, acute or chronic, is one for the most frequent complaints seen by gynecologists (Danielsson, 2003), and often one of the most complex problem to treat as anatomically and embryologically so many organs, muscles and nerves lie in proximity. Innervation to the upper vagina is complex as it derives branches from the spinal nerves S2-S4, pelvic splanchnic nerves,

inferior hypogastric and pelvic plexus. The various causes of pelvic pain and dyspareunia are well-described in the medical literature (Eickmeyer, 2016; Aslan, 2008; Meana, 2015; Ferrero, 2008, Lowenstein, 2004).

Table 38-1 Possible Etiologies of Pelvic Floor Pain or Dysfunction by Medical Specialty

Gynecologic	Gastrointestinal/Genitourinary	Musculoskeletal	Psychological
Vulvodynia	Interstitial cystitis	Low back pain	Anxiety
Dysmenorrhea	Urgency/frequency syndrome	Lumbar radiculopathy	Depression
Endometriosis	Levator ani syndrome	Sacroiliac joint dysfunction	History of abuse
Fibroids	Bowel/bladder incontinence	Coccydynia	
Organ prolapse		Hip disorders	

Table 38-2 Pelvic Floor Musculature Anatomic Origins, Insertions, Innervation, and Function

Muscle	Origin	Insertion	Innervation	Function
Puborectalis	Pubic symphysis	Pubic symphysis	S3 to S5, direct innervation from sacral nerve roots	Raises the pelvic floor
Pubococcygeus	Posterior pubic bone and arcus tendineus	Anococcygeus ligament and coccyx	S3 to S5, direct innervation from sacral nerve roots	Maintains floor tone in upright position
Iliococcygeus	Ischial spine and arcus tendineus	Anococcygeal raphe and coccyx	S3 to S5, direct innervation from sacral nerve roots	Voluntary control of urination
Coccygeus	Ischial spine	Lower sacral and upper coccygeal bones	S3 to S5, direct innervation from sacral nerve roots	Support of fetal head
Piriformis	Anterior sacrum	Posterior surface of greater trochanter	S1 to S2 via nerve to piriformis	Lateral rotation, abduction of thigh; retroversion of pelvis
Obturator Internus	Pelvic surface of ilium, ischium, and obturator membrane	Posterior surface of greater trochanter	L5, S1 to S2 via nerve to obturator internus	Lateral rotator of thigh

Changes associated with aging contribute to painful intercourse in the peri and post-menopausal woman. The vaginal tissue loses its elasticity and natural lubrication is halted due to hormonal and vascular changes.

Even for the most experienced surgeons, pain with intercourse is one of the sequela of hysterectomy, with or without concomitant surgeries. Post-operative dyspareunia can occur due to recurrence of conditions for which the hysterectomy was indicated, post-operative changes, as well as pre-existing pain syndromes. De novo dyspareunia may occur in as many as 2.3% of women after undergoing hysterectomy, although the true incidence may not be known (Rhodes, 1999). Hyperalgesia or allodynia of the vaginal cuff suggest neuropathic dysfunction (Lamvu, 2004). Abdelmonem (2010) reported on a significant difference in the post-operative dyspareunia rate of 20% associated with vaginal hysterectomy for prolapse compared to 5% following total abdominal hysterectomy for other benign reasons. Pelvic organ prolapse per se, can affect sexual function. Women with pelvic organ prolapse will often be offered a vaginal approach to their hysterectomy, which has been **encouraged by the American College of Obstetrics and Gynecology**, along with other concomitant vaginal procedures. The rate of dyspareunia is approximately doubled in vaginal hysterectomy compared to the abdominal route. Pelvic organ prolapse is associated with pelvic discomfort and sexual dysfunction (Dua, 2012). Post-operative dyspareunia after pelvic organ prolapse surgery with native tissue is reported to occur in approximately 14.5 to 36% of women. It is also noted that a vaginal hysterectomy may negatively affect sexual function, although it is unclear if linked to length or caliber (Weber,

2000). Post-operative adhesion formation caused by tissue manipulation during normal surgical procedures can result in pain. Nerve fibers are present within scar tissue even in the normal course of healing. Pain at the apical scar may be secondary to nociceptive sensation or reflect prior chronic pelvic pain. Dense adhesion causing organ immobility may also be associated with pain. Research looking at various risk factors for the development of post-operative chronic pain demonstrate a previous history of pain, anywhere, to be the biggest risk factor (Butrick, 2016). Chronic local or systemic pain syndromes involve central sensitization and increased up-regulation and abnormal sensory processing, and contribute to the emergence of disproportionate pain elsewhere in the body.

Increasingly accepted as an etiology of pelvic pain, dyspareunia, voiding and defecation issues are a dysfunction of the levator ani muscle group, especially the puborectalis and pubococcygeus muscles. Hypertonicity can cause severe proximal (introital), mid and/or deep dyspareunia, as well as discomfort or pain that can last hours or days after intercourse. Other symptoms include pelvic pressure and the sensation that pelvic organs are falling out. Women complaining of significant pelvic pain along with prolapse symptoms often have myofascial pain, out of proportion to the degree or severity of the prolapse. The reported prevalence of levator ani myalgia varies between 9% and 24% depending on the institution, although these women were significantly younger and reported a much higher symptom bother score on standard questionnaires. Also significant is the self-reported increased rate of fibromyalgia (OR 4.4), depression (OR 1.8), use of narcotics (OR 2.5) and prior sexual abuse (OR2.5) (Adams, 2013).

Voiding dysfunctions are common including urgency, frequency and feeling of incomplete bladder emptying, straining with urination and supra-pubic pain.

Defecation problems occur due to a paradoxical contraction of the levator ani muscle, while is should be relaxed. This obstructed defecation causes women to strain forcefully and over years contribute to rectal mucosal prolapse and worsen overall pelvic organ prolapse. This is often interpreted as constipation but does not respond to usual bowel remedies or prolapse repair. Fibers from S2-4 nerves, inferior hypogastric and splanchnic nerves give innervation to the pelvic musculature, pelvic organs and vagina. This complex anatomy helps to explain associated low back and low anterior abdominal pain. Levator ani myalgia and spasms may contribute to, or result from, urethral irritation and/or urinary tract infections. Symptoms of urgency, frequency and feeling of incomplete bladder emptying are common. Over time this leads to straining to void and the development of stress urinary incontinence. A long history of bladder issues, dysuria or dyspareunia may exacerbate pelvic floor spasms further increasing the patient's symptomatology and pain. Treatment includes therapy by experienced physical therapists, specializing in pelvic floor and sacro-iliac disorders, and may include bio-feedback. In addition, medical therapies may include muscle relaxants, neuro-affecting drugs, vaginal Diazepam and intra-muscular injections with local anesthesia, steroids and even Botox. In my practice, I

personally refer 2 to 10 patients per week to pelvic floor therapy for the management of chronic pelvic pain, dyspareunia, voiding or defecation problems associated with levator ani muscle spasms, and/or sacroiliac pain and lumbosacral plexus disorders. Some of these patients have never had pelvic or incontinence surgeries. Some have had a hysterectomy performed in the past for pain but are seeing me for persistent pain, and certainly, the majority of these women have never had any vaginal mesh surgery. All pelvic floor surgeries are associated with commonly known risks such as pelvic pain and dyspareunia, both of which can be temporary or chronic. Dyspareunia was described as a well know and accepted complication of vaginal surgery going back to the 1960s (Francis, 1961).

Painful Bladder Syndrome:

Painful bladder syndrome, including interstitial cystitis are chronic conditions associated with urethral, bladder and pelvic pain, symptoms of urgency and frequency, as well as dyspareunia in 50-90% of women with this condition. Women are five times more affected than men and the prevalence is reported to be approximately 4.3%. Although the exact etiology is unknown, theories include inflammation/injury to the GAG layer composing the inner lining of the bladder, which contributes to decrease pain threshold, bladder compliance and increased irritative voiding symptoms. The immune system response may be implicated as manifested by mast cells found along with nerve fibers in the urothelium along with epithelial dysfunction at the cellular level. One of the most frequent associations is a history of frequent urinary tract infections, although an initial UTI may be implicated in the etiology, no specific bacteria has been implicated. On pelvic examination, 78-85% of patients have associated levator myalgia (Bassaly 2011, Peters, 2007). Symptom exacerbation, or flare-ups are common and can last a few days to weeks. Over time, fear of pain will further contribute to pelvic floor spasms, avoidance of penetration and potentially decreased libido. Treatment involves long term management involving a multidisciplinary approach including dietary modifications, oral medications (antispasmodics, Phenazopyridine-AZO, neuromodulators, antidepressants, antihistamines, Pentosan-Elmiron), pelvic floor physical therapy & intravaginal diazepam, bladder instillations, cystoscopic hydrodistension/treatment of Hunner's lesion, neuromodulation, and other more invasive surgeries. Chronic cystitis, trigonitis or urethritis are also contributors to pelvic pain. The urogenital organs are intimately linked. The bladder, trigone and urethra all rest on the anterior vaginal mucosa and are compressed and stretched during coital activity. This will be compounded by levator ani dysfunction and/or perineoplasty which further reduces the introital diameter.

Stress Urinary Incontinence:

Urinary incontinence increases with age and impacts approximately 30-60% of middle age and older women. Half of these women will have Stress Urinary Incontinence (SUI) as defined by a complaint of involuntary loss of urine on effort or exertion, or on sneezing or coughing as defined by the International Continence Society. Risk factors contributing to the development of

SUI include childbirth, obesity, previous pelvic floor surgery and age. Situations contributing to increased intraabdominal pressure such as obesity, repetitive straining and coughing as well as occupational factors have been implicated. The socio-economic burden of incontinence is high. Included are the costs of medical and surgical therapies but most of monetary burden for patients are the costs of pads and diapers. A year's supply of fitted incontinence diapers can run between $1500-$2000 per year. Health wise, incontinence contributes to depression, reduction of activities and traumatic falls. There is also a burden on society as this contributes to admissions to nursing homes.

Urinary incontinence has a major impact on quality of life and this has led to the development of several surgical options. At a minimum, stress urinary incontinence symptoms are a quality-of-life issues which interfere with a woman's sense of well-being. As urinary symptoms worsen, odors develop along with their associated embarrassment, negative body image, uncomfortable intimacy and even leakage during intercourse leads to decreased interest in intimacy, and eventually social isolation starts to occur. Women gradually forgo trip outings, social gatherings, and even family outings. Women suffering from symptomatic pelvic organ prolapse also start to decrease their level of physical activity and exercise, decreasing their quality of life, but this can also lead to medical problems, weight gain and associated negative impact on overall cardiovascular health.

Modern vaginal pessaries are made of silicone and are an option for both prolapse and urinary incontinence, if the patient can be properly fitted, is willing and able to care for the pessary. To defy gravity and keep the pelvic organs up above the hymen, not only at rest, but during time of straining, lifting, or physical activities, it must be larger than the vaginal introitus. The ability to correctly and comfortably fit a pessary is dependent on the vaginal dimensions and shape. This device rests anteriorly behind the pubic symphysis near the urethro-vesical junction and laterally against the levator ani muscle complex, and for women with pelvic floor dysfunction, causes further spasms and pain. In most situation, due to the size of the pessary and its firmness, intercourse can be difficult with the device in place and women need to be able to remove it or have her partner willing to do so. Since the pessary also needs regular cleaning a woman must be able to remove it, have her partner do so, or be willing to come to her physician's office or have a home care nurse. Despite these cleanings, women are encouraged to insert vaginal estrogen or low-dose antibiotic gel periodically. Without this, most will experience a greenish foul-smelling discharge due to bacterial overgrowth as this pessary resides in a non-sterile environment of the vagina. Women less than 65 years, desire for surgery and advanced posterior prolapse are independent factors for discontinuation (Ninivago, 2016). Despite a well-fitting pessary, previously continent women may become incontinent. One explanation is that once the prolapse is reduced and the vaginal angle repositioned, thus unkinking the urethra, stress urinary incontinence will be more evident. Another, is that mechanically the pessary can put pressure on the bladder causing irritative voiding symptoms, or by compressing directly the urethro-vesical junction, cause incomplete bladder emptying and abnormal voiding issues. Complications from

pessary use include cervical and vaginal mucosa infection, ulceration and erosion of the underlying fibromuscular layer and organs. These incarcerated pessaries have also led to vesico-vaginal and recto-vaginal fistula.

It is no wonder most studies show that despite most women being able to be fitted with a pessary, after one year of use, less than half continue this mode of therapy and opt for a surgical intervention.

For mild stress incontinence occurring with activities, some women are using a strategically placed tampon that would apply slight pressure to the proximal urethra or a least decrease hypermobility. In 2015 the FDA cleared the Poise Impressa, a non-absorbent tampon like device for bladder support that deploys in the vagina, and can be worn for up to 8 hours. It is made of silicone armature, enclosed in a non-absorbent covering made of polypropylene, which does not promote infection.

The traditional standard retropubic surgeries were performed via laparotomy (open abdominal incision) and were found to have a higher success rate than the traditional vaginal anterior colporrhaphies or vaginal needle suspensions. The Burch colpopexy and the pubovaginal sling, designed to suspend the bladder neck, were associated with a longer operating time, higher rates of complications and post-operative voiding dysfunctions and finally a significant longer recovery time. It was not unusual for women to be discharged with a catheter for a few weeks and take a 6 to 8-week convalescence.

The traditional Burch colposuspension has been performed by laparotomy for many decades, but in the early 1990's the introduction of laparoscopy, and more recently robotic technology, have decreased some of the complications associated with an open procedure. The Burch colpopexy has been demonstrated to be more effective than conservative management, medical treatment, vaginal anterior colporrhaphy, needle suspensions and the Marshal-Marchetti-Krantz procedure, which was first performed in the 1950's with sutures directly through the periosteum of the pubic symphysis, and in its day was considered a radically new approach. Although a laparoscopic approach offers a minimally invasive alternative, it is reported to be associated with an 11% ureteral injury rate compared to the open technique. A Cochrane review (Lapitan, 2012) reports a success rate of 68.9%-88% for the Burch colposuspension procedure, The SiSTER trial (Albo, 2007) reports a 3% incidental bladder perforation and a 3.9% rate of wound infection requiring surgical re-intervention. Cure rates decreased significantly for both procedures at 5-7 year follow-up. Long term though, 56% of women demonstrated significant incontinence and only 19% remained dry (Kjolheda, 2005). The open Burch colposuspension is associated with increased voiding dysfunctions compared to midurethral sling procedures (ACOG practice bulletin, 2015 – Ward, 2002), as well as an 8-fold increased risk of developing new or recurrent

prolapse compared to sling procedures (Lapitan, Cochrane review, 2012). There was similar quality of life outcomes, except for emotional and social functioning, vitality and mental health were significantly less improved in the colposuspension group (Ward, 2002). At follow up, Demirici (2001) found occurrence of cystoceles, enteroceles and rectoceles as well as complications including groin or suprapubic pain 6% and dyspareunia 2.7%. Moreover, the performance of a concomitant Burch colpopexy for stress incontinence along with a concomitant posterior colporrhaphy for posterior vaginal prolapse or rectocele was associated with a 38% rate of dyspareunia (Webber, 2000). The open and laparoscopic colpopexy also presents unique risks associated with intra-abdominal surgery.

Pubovaginal slings involve placement of a fascial sling at the proximal urethra/bladder neck, through the retropubic space and attaching it to the anterior abdominal fascia. They have evolved since 1907 when a muscle structure was first described to serve as an additional bladder neck support. In 1914, harvesting of the abdominal fascia was first described. Although various materials have been utilized, including synthetic or biological (autographs: from patients own abdominal rectus fascia, fascia lata, or vaginal as well as allographs: cadaveric fascia, dermis or dura mater, and finally xenograft: derived from porcine or bovine tissue). Freeze-dried biomaterials have lower load failure than solvent dehydrated materials and both have significant thinning and degradation of the sling scaffolding as described by Woudruff (2008). Although rare is a concern for the transmission of prions and other diseases including HIV, hepatitis and Creutzfedt-Jacob from the donor mesh. Porcine dermis or small intestinal submucosa and bovine pericardium are sometimes used. Small intestinal mucosa has less tensile strength than cadaveric fascia and had the high risk of encapsulation.

Currently, the synthetic polypropylene midurethral sling made from polypropylene is the most frequently performed procedure for treating stress urinary incontinence. In attempts to reduce the invasiveness or the abdominal surgeries, such as the Burch and autologous slings, attempts at different attachments have included various materials including bone anchors which had an increase in morbidity and are rarely used anymore. The comorbidity of thigh pain for fascia lata slings is significant. Brown (2000) published that all patients undergoing fascia lata harvest had thigh pain at 2 weeks and 11% still had persistent pain at 6 weeks post-operatively. Complications of tendinitis (5%) and numbness (20%) have been reported (Latini, 2014). Abdominal harvesting has its own set of complication, to include wound infection, nerve damage resulting from harvesting or closure of the fascia, and incisional hernia. The literature is populated with a wide range success rates 46% to 97% depending on the definition of success as patient derived responses of cure are often less than physician reported outcomes. Autologous and cadaveric sling studies are often limited by low follow-up rates and short-term follow-up. De-novo urinary urgency incontinence is reported to be 2% up to 20.8% (Hassouna, 1999). Using frozen or freeze-dried allografts, success vary between 63.4% (Richter, 2003) and Walsh (2002) reported a success rate of 94% at 1 year, but only had 31 patients. Again, de-novo urgency incontinence occurred between 3-36% (Handa, 1996).

One of the largest randomized trials, the SiSTER trial reported in the New England Journal, compared the pubovaginal sling to Burch colposuspension (Albo, 2007). They showed that overall composite success (no self-reported incontinence, 15g pad test/24 hours and no medical or surgical treatment) was superior for the pubovaginal sling at 47% compare to 38% for the colposuspension, but at the expense of much increased rates of urinary tract infections (48% vs 32%), voiding dysfunctions/obstructed voiding (14% vs. 2%) and urge incontinence requiring treatment (27% vs 20%). Post-operative voiding dysfunction may present as urinary frequency, urgency, reduced urinary flow and feeling of incomplete bladder emptying. These women may also present with recurrent urinary tract infections, prolonged suprapubic pain and painful micturition. There are no absolute criteria to predict which woman will be at risk and studies have published conflicting results: Valsalva voiding or detrusor underactivity may (Weinberger, 1995) or may not (McLennan, 1998) be predictive. Transient urinary retention is common after pubovaginal sling, so many patients will be managed conservatively with intermittent self-catheterization or suprapubic catheters for a few weeks to a few months. In these cases of symptomatic obstructed voiding, sling incision and/or ureterolysis is often necessary and is reported associated with return of stress incontinence in 0 to 19% (Goldman, 1999). Failures of urethrolysis may result from scarring and fibrosis and/or patient voiding dysfunction. These may require a second surgical procedure. Persistent and refractory overactive bladder symptoms are reported in 50% of patients and significantly impact quality of life (Starkman, 2008). Reports of persistent urinary retention after pubovaginal slings are not rare. The AUA Stress Urinary Incontinence Clinical Guidelines (1997) mentions that prolonged urinary retention of more than four weeks was 8%, and the risk of permanent urinary retention "generally does not exceed 5%". This means that women must self-catheterize or live with a urethral or suprapubic catheter. Complications related to the surgical procedure as reported by Anger (2007) include urinary tract infections (33.6%), bowel injury or obstruction (6.6%), transfusions (2-7%) and general medical complications more often associated with increased age and medical pre-existing comorbidities.

Noticeably absent is data on sexuality, dyspareunia and overall quality of life assessment from most pubovaginal studies. Certainly, the rates of complications of the traditional pubovaginal sling are significant, but are deemed acceptable in women who have failed previous SUI surgeries, have intrinsic sphincter insufficiency and had urethral complications or in patients needing concomitant urethral reconstruction such as diverticulum or fistulas and incontinence surgery.

Synthetic Midurethral Slings:

General surgeons began attempting to repair hernias with mesh in the 1950s, which started the evolution of various meshes and techniques using mesh repairs to provide more consistent and durable repairs in various parts of the body. The goal with using mesh in hernia repairs was to provide a more durable and consistent repair that surgeons and patients were not achieving with

native tissue repairs. Gynecologic surgeons adapted mesh to the pelvic space to treat SUI and POP abdominally for decades to reduce the failure or recurrence rates seen with native tissue repairs. To meet this need for a more durable repair, Ethicon and other companies began to supply mesh for use in the pelvic surgery. Throughout this time, surgeons began performing urogynecologic surgeries, including for stress urinary incontinence, using synthetic slings. Iglesia (1997) describes some of the commonly known complications that were reported with various synthetic bladder neck slings.

As described in the Librojo declaration, Ethicon submitted to the FDA its application for Prolene in January 1966 as a new drug, which included required studies of the polypropylene suture. After a 3-year review, after meeting the requirements of the FDA, the agency concluded that Prolene was safe and effective for its intended use, and granted approval in April 1969. Prolene sutures then rapidly became the suture of choice for various surgery involving tissues that required permanent sutures. Various changes to the labeling, approved by the FDA were made over the years to include warnings on "minimal transient acute inflammatory reaction", "resists involvement in infection" and that "it is not subject to degradation or weakening by the action of tissue enzymes". Such statements were supported by Ethicon submitted as part of the NDA and various supplements, as well as published medical literature.

In 1976, the FDA reclassified Prolene as a Class III medical device. Since it already had been used safely for more than a decade and because it had been approved as safe and effective by the FDA, it automatically had pre-market approval by the FDA.

In 1982, the FDA recommended that surgical meshes be classified into class II and this was upheld in 1988. By then, various surgical mesh had been widely used for more than two decades.

In 1990, polypropylene sutures were down classified to Class II. Prolene mesh, knitted form the same monofilaments of Prolene, was also marketed after 1969 and because the FDA did not classify it as a drug, it also was included as a pre-amendment device.

The Synthetic midurethral sling developed in the mid 1990's was a significant improvement over those traditional surgeries as they could be performed as an out-patient surgery, with reduced surgical time, using minimal incisions, and with an acceptable morbidity and much quicker recovery time. In 1995, Ulmsten and colleagues reported on a 2 year midurethral sling using a retropubic synthetic mesh named tension free tape. The Amid class 1 Prolene mesh would be positioned at the level of the midurethra and left in place without the need for difficult suturing or anchors.

In 1996, Ethicon submitted a 510(k) for Modified Prolene surgical mesh based on the predicated Prolene mesh and obtained clearance in August of the same year. Throughout the 1990s, Professor Ulmsten published his early clinical results on an innovative tension-free procedure using a variety of synthetic meshes, such as GoreTex and Mersilene, before finding the best success with Ethicon's Prolene polypropylene sling. TVT was cleared in Europe in 1997.

In 1998, the FDA cleared the TVT device under 510(k). Since that time, other manufacturers have developed and marketed similar Amid Type I, polypropylene, monofilament, macroporous midurethral slings.

In December 2003, Ethicon's TVT-O received 510(k) clearance from The FDA based on the predicated TVT device.

Since then, there have been over 2000 articles published in the medical literature on the synthetic midurethral sling, which has been studied in systematic reviews and meta-analyses, including multiple cochrane reviews. The synthetic polypropylene midurethral sling has been the most studied anti-incontinence procedure, surpassing all other previous traditional surgeries (Nager, 2014).

Initially developed as a retropubic approach, the introduction of the sling mesh is accomplished bottom-up (TVT), but it can also be performed top-down (SPARC). Comparing the two, (Ogah, 2011) found that the bottom up approach will result in significantly less bladder perforations (4.7% vs. 8.5%), fewer vaginal mesh exposures or erosions (0.7% vs. 3.5%) and greater subjective (85% vs. 77%) and objective cure rates (92% vs. 87%). These conclusions were echoed by the 2015 Cochrane review. Many meta-analyses and systematic reviews have been conducted comparing midurethral slings with traditional surgeries (Rehman, 2001; Novara, 2010 Ogah 2009; Ogah 2011; Ford, 2015; Schimpf, 2014), concluding that midurethral slings resulted in less urinary tract symptoms and less reoperations compared to the pubovaginal sling. A literature review from Cox (2013) compared the results of various meta-analyses evaluating midurethral slings.

Table 1 | Meta-analyses of midurethral slings versus traditional procedures for stress urinary incontinence

Study	Comparison	Subjective success at 12 months	Objective success at 12 months
Rehman *et al.* (2011)[25]	Pubovaginal fascial sling vs midurethral sling	Equal success ($n=693$) RR 0.97 (95% CI 0.78–1.20)	Equal success* ($n=160$) RR 1.29 (95% CI 0.45–3.71)
Novara *et al.* (2010)[27]	Midurethral sling vs Burch colposuspension	Equal success ($n=400$) OR 0.79 (95% CI 0.52–1.21; $P=0.27$)	Favoured midurethral sling ($n=528$) OR 0.38 (95% CI 0.25–0.57; $P=0.0001$)
Novara *et al.* (2010)[27]	Midurethral sling vs pubovaginal sling	Equal success ($n=281$) OR 1.28 (95% CI 0.74–2.23; $P=0.38$)	Equal success ($n=473$) OR 0.8 (95% CI 0.51–1.26; $P=0.35$)
Ogah *et al.* (2009)[4]	Midurethral sling vs pubovaginal sling	Equal success ($n=599$) RR 1.03 (95% CI 0.94–1.13)	NR
Ogah *et al.* (2009)[4]	Midurethral sling vs open Burch colposuspension	Equal success ($n=729$) RR 0.96 (95% CI 0.90–1.03)	Equal success ($n=468$) RR 1.04 (95% CI 0.94–1.14)

Table 2 | Meta-analyses of midurethral slings versus laparoscopic Burch procedure

Study	Comparison	Follow-up (months)	Subjective success	Objective success
Ogah *et al.* (2009)[4]	Midurethral sling vs laparoscopic Burch colposuspension	12	Equal success ($n=434$) RR 1.11 (95% CI 0.99–1.24)	Favoured midurethral sling ($n=513$) RR 1.15 (95% CI 1.06–1.24)
Dean *et al.* (2006)[32]	Laparoscopic colposuspension vs midurethral sling	18	Equal success ($n=327$) RR 1.12 (95% CI 0.98–1.29)	Favoured midurethral sling ($n=534$) RR 1.16 (95% CI 1.07–1.25)

With conventional surgery, retention lasting more than one month was reported to be on average 8% (1-15%) compared to 3% (2-4%) with early experience with midurethral slings. De novo urgency incontinence has been reported to be approximately 10% (3-20%) with conventional surgeries compared to 6% (3-10%) for mid urethral sling. These rates were almost doubled when concurrent POP surgeries were performed. The rates of symptomatic post-operative urinary urgency are approximately three times less with midurethral sling compared to pubovaginal slings.

In 2001, the transobturator approach was developed to further reduce the intra-operative risks of lacerations to the bowel, bladder and well as vascular injuries. The TVT-O was found to have a high cure rate at 12 months (91%) with less than 10% voiding dysfunction. No urethral or bladder perforation occurred during the surgeries and no post-op mesh erosions were recorded. This was also confirmed in a longer follow up (Waltregny, 2006 and 2009). Here as well, there are two approaches: the inside out (as in the TVT-O) and the outside in. Both have shown equal rates of objective and subjective cure rates, but the inside out technique is associated with less voiding difficulty and less bladder perforations (Novara, 2010; Latthe, 2010; Ford 2015). In a meta-analysis of prospective randomized trials, Latthe (2009) compared a total of 2122 women who underwent retropubic, versus 1144 with transobturator outside-in, and 1530 women with the inside-out (TVT-O) midurethral sling. Overall subjective and objective cures were similar, bladder and vascular injuries were less with the obturator compared with the retropubic approach. Overall, comparing the inside-out to outside-in, both have similar efficacy and safety profiles, but TVT-O has been associated with lower rates of voiding dysfunction.

In their Guideline for the Surgical Management of Female Stress Urinary Incontinence 2009 Update, the AUA also reported on complications as they relate to pain and sexual dysfunction. Grouping all retropubic suspensions, pain varied from 3-12% and sexual dysfunction between 2 to 6%. Grouping pubovaginal slings, pain was varied from 1-35% and sexual dysfunction between 3-16%. Grouping synthetic midurethral slings, pain varied from 0-3% and sexual dysfunction between 0-4%, with most women reporting an overall significant improvement compared to baseline (Abdel-Fattah, 2010). The literature has consistently shown that leg or groin pain more commonly associated with transobturator midurethral sling is usually transient, with most resolving within a few weeks (Ford, Cochrane review, 2015), using conservative measures. Reports of chronic groin or leg pain with TVT-O are rare, especially in the long-term TVT-O studies (Laurikainen 2014, Anthansiou 2014, Serati 2012, Liapis 2010). A one year prospective RCT comparing TVT-Abbrevo to TVT-O found lower rates in groin pain in the TVT-Abbrevo group at postoperative day 0 and day 1, but no difference thereafter (De Leval 2011). Midurethral slings offer a greater improvement in quality of life domains compared to Burch surgeries (Ogah, 2009).

Comparing the retropubic vs. the transobutrator approach has been the subject of many debates but looking at meta-analyses and RCT studies (Ogah, Cochrane data base 2009; Ford, Cochrane 2015). Success rates are similar with slight advantage of the retropubic approach regarding the objective cure rates and possibly advantageous in cases of intrinsic sphincter deficiency. The advantages of the transobturator approach include decreased bladder perforations (0.3% vs. 5.5%) but this rate is significantly higher using the retropubic approach in patients with previous incontinence surgery. There is decreased post-operative voiding dysfunctions (0.8-4% vs. 7-12.2%) and less required surgical re-intervention. The retropubic midurethral sling has been associated with supra pubic pain in 1.7%, but the transobturator sling resulted in groin pain in 6-12% of patients, which was temporary with no long-term sequelae in most patients (Tommaselli, 2014). Overall the complication rates associated with retropubic midurethral slings are higher compared to the transobturator approach (Richter, 2010). The retropubic approach was associated with more vaginal mesh exposures, along with premenopausal status and previous bariatric surgery (Linder, 2016).

Longer term studies also support the use of synthetic midurethral slings. A retrospective case-control study involving **2123** women undergoing a midurethral sling (retropubic or transobturator) over a span of 10 years, identified 27 patients (1.3%) with vaginal mesh erosion needing surgical correction. In another case control study (Unger, 2016), reviewing **3307** women receiving a midurethral sling over a 10-year period, found an overall 2.7% revision rate for various indications, with a median time 7.8 months (2.3 to 17.9 months). A **17-year** prospective study described the TVT operation as durable with 87% subjectively cured or significantly improved and a high satisfaction rate (Nilsson, 2013).

The 2009 Cochrane review (Ogah, 2009) concluded that midurethral slings were as effective as the more invasive, traditional continence surgeries and that major complications such as nerve, bowel or major vascular injuries, pelvic hematoma, necrotizing fasciitis, abscess and death are uncommon. These conclusions are also maintained in the 2015 Cochrane review of midurethral slings (Ford, Rogerson, Cody, Ogah, 2015). The 2016 Cochrane review of open retropubic colposuspension for urinary incontinence echoes these conclusions and stated that open retropubic colposuspension was regarded as the gold standard for the treatment of urinary stress incontinence until the arrival of the minimally invasive midurethral sling (Lapitan, 2016)

It is now undeniable that midurethral slings have a very acceptable risk/benefit profile. According to the American Urogynecologic Society (AUGS) and the Society of Urodynamics, Female Pelvic Medicine and Urogenital Reconstruction (SUFU), "**full length midurethral slings, both retropubic and transobturator, have been extensively studied, are safe and effective relative to other treatment options and remain the leading treatment option and current gold standard for stress incontinence surgery." Additionally, "Over 3 million MUS have been placed worldwide and a recent survey indicates that these procedures are used by > 99% of AUGS members."** The AUGS/SUFU position statement on synthetic midurethral slings was also endorsed by ACOG, SGS, AAGL, The National Association for Continence (NAFC), and Women's Health Foundation (WHF). The American Urologic Association (AUA) issued a position statement in 2011 supporting synthetic midurethral slings, stating: "Advantages include shorter operative time/anesthetic need, reduced surgical pain, reduced hospitalization, and reduced voiding dysfunction. Mesh-related complications can occur following polypropylene sling placement, but the rate of these complications is acceptably low. Furthermore, it is important to recognize that many sling-related complications are not unique to mesh surgeries and are known to occur with non-mesh sling procedures as well." Other professional organizations such as ACOG, IUGA, , EAU, and NICE have also endorsed the full-length polypropylene midurethral slings as the standard of care for treating stress urinary incontinence in a variety of publications, guidelines, and position statements. The EU Commission issued the SCENIHR Report in 2015 and determined that the polypropylene synthetic midurethral slings are "currently considered the standard of care" for the treatment of SUI. They also noted the lack of evidence to support the use of other mesh materials, specifically noting the lack of evidence evaluating PVDF mesh.

The GYNECARE TVT Obturator System IFU from launch in 2004 to 2015 includes the following warnings and precautions as well as adverse reactions specific to the surgical implant:

ADVERSE REACTIONS

- Punctures or lacerations of vessels, nerves, bladder, urethra or bowel may occur during needle passage and may require surgical repair.
- Transitory local irritation at the wound site and a transitory foreign body response may occur. This response could result in extrusion, erosion, fistula formation or inflammation.
- As with all foreign bodies, PROLENE mesh may potentiate an existing infection. The plastic sheaths initially covering the PROLENE mesh are designed to minimize the risk of contamination.
- Over correction, i.e. too much tension applied to the tape, may cause temporary or permanent lower urinary tract obstruction.

The warnings also noted "Transient leg pain lasting 24-48 hours may occur and can usually be managed with mild analgesics." Pelvic floor surgeons would know of the risks associated with any surgery including injury to pelvic and adjacent organs, pain and dyspareunia by way of their basic medical education and training. They would also know that pain and dyspareunia are potential risks from infection, inflammation, adhesion formation, fistula formation, erosion, and extrusion and that these potential complications may need reparative surgery. In addition to Ethicon's IFU, Surgical Technique Guide and Professional Education, the medical literature also describes the risks associated with incontinence surgery, including the potential complications related to foreign bodies, such as erosion or exposure.

Complications of TVT-O are known, acceptable and are often easily manageable. Even complications requiring surgical management are often successful without having to dissect the entire arms of the mesh. This is consistent with my clinical experience and the medical literature describing resolution of symptoms after intervention. Serious life threatening complications are rare. Predictors of early postoperative voiding dysfunction have been investigated. In a retrospective cohort from 5 academic centers looked at 402 patients. Of the 317 women who underwent a retropubic sling, 22% failed their voiding trial. Of the 82 with a transobturator sling, 24% failed and 3 had a single incision, none failed. They determined that these women were more likely to have a voiding type other than detrusor contraction but more likely to have detrusor overactivity diagnosed pre-operatively and have an elevated post void residual volume. The authors also noted that of the women who initially failed their first voiding trial, 11.8% had further acute retention as compared with 3.9% who passed their first post-operative trial.

Millions of minimally invasive sling have been performed and the data is impressive. In a study of **41,604** women who underwent pelvic organ prolapse and/or incontinence surgeries with mesh, the rate of mesh erosion was 1.16% in the sling group, 1.9% in both native tissue repair with sling and vaginal mesh repair without sling, and 2.7% in the group who underwent both vaginal mesh and sling surgery. All mesh exposures occurred within less than 1 year after the index surgery (Chunghtai, 2016).

Follow-up data was analyzed on **188,454** women who underwent a sling insertion for SUI. At 1 year, the risk the risk of revision or removal was 2.2%. The risk increased to 3.2% at 4 years, with a 9-year cumulative risk of 3.7% (Jonsson Funk, 2013). Welk (2015) identified **59,887** women who underwent mesh-based procedure for SUI during a 10-year period, in the province of Ontario, Canada. He reported an incidence of 2.2% of mesh removal or revision after receiving their initial mesh implantation for SUI.

In an evaluation of postoperative mesh complication, Miklos (2016) reports on 445 patients underwent mesh removal from 2011 to 2013, from slings (56.5%) and pelvic prolapse mesh (43.5%) including sacrocolpopexy and transvaginal mesh. Pain was the most common complaint. They conclude that "overall, sling, TVM, and sacrocolpopexy mesh removal are safe procedures when performed by experienced surgeons. Pastore (2016) evaluates sexual function after TVT-O versus single incision sling. They found the overall complete and improved success to be similar in both groups associated with significant improvement of sexual function on validated questionnaire (FSFI). These improvements were also reported after TVT-O Sling surgeries (Murphy, 2008 - Elzevier, 2008 – Xu 2011). Improvement of sexual function after midurethral sling is multifactorial and may be associated to the disappearance of coital incontinence, improved body image and increased ability to achieve orgasm (Sarreau, 2015). A secondary analysis of the 597 patients enrolled in the TOMUS trial, evaluated pain complications after surgery for stress urinary incontinence. There was no difference in any overall surgical pain, severity of pain with activity or pain medication requirements. Suprapubic pain was more prevalent in retropubic slings at 2 weeks compared to the transobturator outside-in or TVT-O, but not thereafter. Groin pain was more prevalent in both the transobturator groups at 2 and 6 weeks, but at 6 months there was no statistical difference, as the presence of groin pain was 1.1% in the transobturator and 0.7% in the retropubic group. There was no difference between the groups in the prevalence of vulvar pain at 2 weeks, 6 weeks and 6 months, but the severity at 2 weeks post-op was worse in the retropubic group. At 6 weeks resolution of all surgical pain was similar. Comparing the Outside-in (Monarc) to the inside-out (TVT-O), the odds of any surgical pain were no different at 2 ant 6 weeks. The authors conclude that approximately 70% of pain occurring after mid urethral sling will resolve at 2 weeks and 90% by 6 weeks (Thomas, 2016). In another analysis of the TOMUS trial, there was a significant improvement of sexual function related to improvements in dyspareunia, decreased coital incontinence and decreased fear of coital incontinence. Their reported rate of dyspareunia pre op was 38% and was 27% at 12 months (Zyczynski, 2012). The urinary Incontinence Treatment Network reported overall satisfaction with midurethral slings to be 85.9% for the retropubic approach and 90% for the transobturator approach (TOT and TVT-O) (Wai, 2013).

It is important to remember is that dyspareunia and pelvic pain are common conditions in the general population. A WHO systematic review (Lathe, 2006) estimates that the world-wide

prevalence of chronic pelvic pain is 2-24% and 1 in 5 women between the ages of 18-50 report pelvic pain longer than 1 year's duration (Howard, ACOG bulletin 2004). Thus, many women have pelvic pain and dyspareunia before undergoing TVT-O, and studies have demonstrated improvement in sexual function after TVT-O. Some studies suggesting 40-50% of women have some form of dyspareunia or chronic pelvic pain at some point in their lives, regardless of whether they have ever sought surgical treatment for pelvic organ prolapse or stress urinary incontinence using mesh. These complications have been documented in the literature well before TVT-O became available.

No matter the approach, all gynecologists are or should be aware of the surgical risks such as bleeding, infection, injury to nerves, organs and vessels, and post-operative risks including scarring, wound complications, painful intercourse (short and long term), pelvic pain (limited or chronic), urinary or bowel problems and the need to re-operate. All those risks are addressed in the medical literature and taught in residency and fellowship programs.

On October 20, 2008, the FDA issued Public Health Notification, to surgeons, practitioners, and consumers regarding the use of mesh from a wide range of manufacturers for the repair of pelvic organ prolapse and stress incontinence.

FDA Public Health Notification: Serious Complications Associated with Transvaginal Placement of Surgical Mesh in Repair of Pelvic Organ Prolapse and Stress Urinary Incontinence

Issued: October 20, 2008

Dear Healthcare Practitioner:

This is to alert you to complications associated with transvaginal placement of surgical mesh to treat Pelvic Organ Prolapse (POP) and Stress Urinary Incontinence (SUI). Although rare, these complications can have serious consequences. Following is information regarding the adverse events that have been reported to the FDA and recommendations to reduce the risks.

Nature of the Problem

Over the past three years, FDA has received over 1,000 reports from nine surgical mesh manufacturers of complications that were associated with surgical mesh devices used to repair POP and SUI. These mesh devices are usually placed transvaginally utilizing tools for minimally invasive placement.

The most frequent complications included erosion through vaginal epithelium, infection, pain, urinary problems, and recurrence of prolapse and/or incontinence. There were also reports of bowel, bladder, and blood vessel perforation during insertion. In some cases, vaginal scarring and mesh erosion led to a significant decrease in patient quality of life due to discomfort and pain, including dyspareunia.

Specific characteristics of patients at increased risk for complications have not been determined. Contributing factors may include the overall health of the patient, the mesh material, the size and shape of the mesh, the surgical technique used, concomitant procedures undertaken (e.g. hysterectomy), and possibly estrogen status.

Recommendations

Pelvic floor surgeons were the target audience of this notification and would have been expected to read and consider this notice. Further, this notice was also discussed in a variety of other publications in the medical literature as well as Ethicon's Professional Education.

The FDA's Public Health Notification of 2008, warned surgeons of risks such as: erosion of the mesh "through the vaginal epithelium, infection, pain, urinary problems, and recurrence of prolapse and or incontinence." Additionally, the FDA notice warned that "there were also reports of bowel, bladder, and blood vessel perforation during insertion. In some cases vaginal scarring and mesh erosion lead to significant decrease in patient quality of life due to discomfort and pain, including dyspareunia". Further, FDA recommended that physicians should:

- •Obtain specialized training for each mesh placement technique and be aware of its risks,
- •Be vigilant for potential adverse events from the mash especially erosion and infection,
- •Watch for complications associated with the tools used in transvaginal placement, especially bowel bladder and blood vessel perforations,
- •Inform patients that the implantation of surgical mesh is permanent and that some complications associated with the implanted mash may require additional surgery that may or may not correct the complication.
- •Inform patients about the potential for serious complication and their effect on the quality of life including pain during sexual intercourse, scarring, and narrowing of the vaginal wall.
- •Provide patients with a written copy of the patient labeling from the surgical mesh manufacture, if available.

A reasonably prudent pelvic floor surgeon performing incontinence and prolapse surgeries would have already been aware of the potential for these complications to occur with mesh, but would have been put on notice of the frequency of those complications outside of what was already reported in the peer-reviewed medical literature.

Patient brochures are intended to help provide an overview of the medical condition and help to initiate the conversation between the surgeon and the patient about treatment options. The TVT-O Patient Brochure that was available to surgeons in 2008, following the FDA's October 20, 2008 Public Health Notification, discussed risks of the Gynecare TVT Family of Products in the "What are the risks?" section of the Patient Brochure, which states:

> **What are the risks?**
>
> "All surgical procedures present some risks. Complications associated with the procedure include injury to blood vessels of the pelvis, difficulty urinating, pain, scarring, pain with intercourse, bladder and bowel injury. There is also a risk of the mesh material becoming exposed. Exposure may require treatment. For a complete description of the risks, see the attached product information
>
> "Synthetic mesh is a permanent medical device implant. Therefore, you should carefully discuss the decision to have surgery with your doctor and understand the benefits and risks of mesh implant surgery before deciding how to treat your condition."

> GYNECARE TVT Family of Products Tension-Free Support for Incontinence
> **Essential Product Information for Patient**
>
> INDICATIONS
>
> GYNECARE TVT Family of Products…are intended to be used in women as suburethral slings for the treatment of stress urinary incontinence (SUI).
>
> WARNINGS & PRECAUTIONS
>
> - Do not use the GYNECARE TVT Family of Products for patients who are anti-coagulation therapy.
> - Do not use the GYNECARE TVT Family of Products for patients who have a urinary tract infection.
> - Bleeding or infection may occur post-operatively.
> - Transient pain lasting 24-48 hours may occur and can usually be managed with mild analgesics after GYNECARE TVT Obturator System.

- Since no clinical information is available about pregnancy following sub-urethral sling procedure with the GYNECARE TVT Family of Products, the patient should be counseled that future pregnancy may negate the effects of the surgical procedure and the patient may again become incontinent.
- Since no clinical information is available about vaginal delivery following sub-urethral sling procedure with the GYNECARE TVT Family of Products, in case of pregnancy, delivery via cesarean section should be considered.
- Post-operatively, refrain from heavy lifting and/or exercises (e.g. cycling, jogging) for at least three to four weeks and to refrain from intercourse for one month. The patients can usually return to other normal activity after one or two weeks.
- Contact your surgeon immediately if there is burning sensation during urination, unusual bleeding, problems voiding or other problems.

ADVERSE REACTIONS

- Punctures or lacerations or injury to vessels, nerves, bladder, urethra, or bowel may occur during instrument passage and may require surgical repair.
- Transitory local irritation at the wound site and a transitory foreign body response may occur. This could result in extrusion, erosion, fistula formation, or inflammation.
- Improper placement of the TVT device may result in incomplete or no relief from urinary incontinence or may cause urinary tract obstruction.

Ethicon communicated the above-mentioned warning language, which includes risks that are well known to physicians and pelvic surgeons. The communication of these risks and benefits appears to be reasonable, comprehensive and proper. It would be almost impossible for a manufacturer to list the exact incidence and severity of all the possible complications including mesh exposure, recurrence, urinary problems, and various other complications that are well documented in the medical literature. Materials like this cannot summarize the vast body of available medical literature, and it is up to the operating surgeon, consistent with his or her training, experience, continuing education and up to date literature, to come to discuss the options for their individual patient and have an informative process with her.

It is my opinion, to a reasonable degree of medical certainty, that the applicable TVT-O IFUs appropriately warned pelvic surgeons of the potential risks and complications specific to the TVT-O. Pelvic floor surgeons who would have the licensing, credentials, and privileges to perform incontinence surgeries, including the TVT-O, would be aware of the commonly known risks and complications that can occur with any pelvic surgery. These include but are not limited to: pain and dyspareunia, both of which can be short term or chronic, and voiding dysfunctions.

Pelvic floor surgeons would be aware of such risks, and should be confident in their ability to manage complications from the procedures they feel competent to perform, based on their medical training, medical literature, their clinical experience, professional education, and through the TVT-O IFUs.

The FDA provided an update on surgical mesh in July 2011. It determined "that serious complications are not rare", contrary to what was stated in the 2008 *PHN*, and "transvaginally placed mesh in POP repair does not conclusively improve clinical outcomes over traditional non-mesh repair." This health notification did not relate to mesh used for stress urinary incontinence.

In response to the FDA's communication, in November 2011, the American Urological Association (AUA)'s position statement that "certain patients may benefit from mesh techniques" and the use of mesh should be a choice made after a careful discussion between surgeon and patient. Better data are needed to determine the appropriate role of vaginal mesh technique in the treatment of POP. It is also important "that many of these complications are not unique to mesh surgeries and are known to occur with non mesh POP procedures as well". The AUA in 2011 stands by their 2009 AUA guideline for the Surgical Management of Stress Urinary Incontinence which concluded that "synthetic slings are an appropriate treatment for women with stress incontinence with similar efficacy but less morbidity than conventional non mesh sling techniques".

In 2012, the consensus of the 2nd IUGA grafts round table acknowledged the large number of traditional techniques of pelvic surgery with many variations from one surgeon to another, with no available data to achieve standardization. They recognized the need for tissue reinforcement and established patient risk factors where mesh could potentially be beneficial. The also concluded that "the main factor for the development or persistence of problematic post-operative pain is the presence of pain preoperatively".

In March of 2013, the AUGS' position on restriction of surgical options for pelvic floor dysfunction stated that "A complete restriction on the use of surgical mesh safety was not the intent of the FDA communication". The decision on surgical alternatives should be made by the patient and her surgeon. "A ban on surgical mesh would prohibit the surgical studies mandated by the FDA and recommended by the NIH, ACOG and AUGS. In some circumstances, transvaginal mesh for pelvic organ prolapse may be the most appropriate surgical option… Any restriction of mesh slings for stress urinary incontinence is clearly not supported by any professional organization or the FDA… Instead of a ban on mesh we recommend the implementation of credentialing guidelines so that mesh procedures are performed by qualified surgeons".

Even on the FDA's web site was stated in 2013 that "the safety of multi-incision slings is well established in clinical trials that followed patients for up to 1 year." (FDA, 2013 Considerations about Surgical Mesh for SUI). The FDA also noted that the most common complications reported for surgical mesh slings for SUI repair, include: "pain, mesh erosion through the vagina (also called exposure, extrusion or protrusion), infection, urinary problems, recurrent incontinence, pain during sexual intercourse (dyspareunia), bleeding, organ perforation, neuro-muscular problems and vaginal scarring. Many of these complications require additional medical intervention, and sometimes require surgical treatment and/or hospitalization." As discussed throughout my report, the FDA further noted that "[w]ith the exception of mesh erosion, the above complications can occur following a non-mesh surgical repair for SUI."

AUGA and SUFU published a joint positions statement on mesh midurethral slings in January 2014: **"The Polypropylene mesh mid urethral sling is the recognized worldwide standard of care for the surgical treatment of stress urinary incontinence". "The procedure is safe, effective and has improved the quality of life of millions of women".** "The monofilament polypropylene mesh midurethral sling is the most extensively studied anti-incontinence procedure in history". "The FDA has clearly stated that the polypropylene midurethral sling is safe and effective in the treatment of stress urinary incontinence".

In June 2016, AUGS revised their position on mesh, stating **"we are concerned that the multimedia attention has resulted in confusion, fear and an unbalanced negative perception regarding the mid-urethral sling as treatment for stress urinary incontinence" "Polypropylene is safe and effective as a surgical implant".** It has demonstrated long term durability, safety and efficacy for stress urinary incontinence for 17 years (Nilsson, 2013). "Polypropylene mesh has helped millions of women with stress urinary incontinence regain control of their lives by undergoing a simple outpatient procedure". "In the past, concerns over failure and invasiveness of surgery caused a substantial percentage of incontinent women to live without treatment". **"One of the unintended consequences of this polypropylene mesh controversy has been to keep women from receiving any treatment for stress urinary incontinence". "This procedure is probably the most important advancement in the treatment of stress urinary incontinence in the last 50 years".**

The FDA's decision in 2016 to reclassify mesh from Class II to Class III was foreseeable. This order does **not** affect full length mesh used for stress urinary incontinence or abdominally placed mesh. It does require all new products to submit pre-market approval application and orders manufacturers of current products to submit post-market analysis within 30 months.

The FDA, in January 2017, issued a final reclassification order regarding surgical instruments for use with urogynecologic surgical mesh from Class I to Class II. This includes needle passers, trocars, needle guides and various tissue anchors used in vaginal or abdominal pelvic prolapse surgery and incontinence surgery. Some of these devices, in use for years, have dual properties for use with vaginally or abdominally placed mesh, and sutures for native tissue repair.

In addressing the FDA's 2011 statement that "serious mesh complications are not rare", one must define what constitute a serious adverse event. These include death or life threatening complications, those that require inpatient hospitalization or increased length of stay of more than 24 hours and complications resulting in disability or permanent damages with significant impairment of conducting normal life functions or an intervention required to prevent any of the above. Most vaginal mesh exposure after sling surgery do not constitute a serious complication as approximately 50% will be treated with vaginal cream and the remainder will be treated by excision in the office or in a surgical suite, many as outpatients.

The IFUs for TVT-O list the complications that are specific to the use of the device. Mesh degradation, chronic inflammation, and cytotoxicity are not considered complications. I have not seen in my practice or in the peer-reviewed medical literature any clinical significance attributed to alleged degradation or cytotoxicity of either TVT or TVT-O. The potential for "degradation of the polypropylene which weakens the mesh to the point that it literally falls apart during dissection" (Ostergard, 2016) is contrary to his own theory of how the mesh reacts within the body, migration of cells in the interstices, collagen and scarring. With new understanding of the process to clean explanted mesh, the previously seen "flakes" on electron microscope attributed to degradation are washed away revealing a smooth surface. If there was degradation, the cracked surfaces seen on the blue fibers would have been blue, not white and once removed, the original fiber would have been pitted or had some residual irregularity on the surface (Ong, 2016; Thames 2016). The authors noted in the disclosure of the published study that they have provided litigation consulting services to Ethicon, Inc. The authors concluded, based on well-designed methodology and testing, that "[o]ur effective cleaning of explanted Prolene meshes and subsequent analyses showed that they did not degrade in vivo, confirming the in vivo stability of properly formulated polypropylene. Instead, the cracked layer that some researchers have identified as degraded Prolene is an adsorbed protein–formaldehyde coating, resulting from the well-established formalin–protein fixation process, which occurs immediately upon placing an explant in formalin." Mesh weakening and falling apart is contrary to the massive documentation in the literature, as well as the clinical experience and surgical success using polypropylene sutures or mesh. If polypropylene mesh behaved in this manner, weakened and fell apart, abdominal walls would be bulging out and hernia mesh would not be considered as standard of care for most hernia repair. If polypropylene behaved in this manor, vaginal apexes would be descending at an alarming rate and sacrocolpopexy would have never been considered for gold standard in level 1 suspension. If polypropylene behaved in this manner, millions of women would suddenly return to urethral hypermobility and stress urinary incontinence. Many

of my colleagues, as well as myself have revised, transected and resected polypropylene slings and meshes and have never encountered this "degradation" after primary insertion of mesh. I have also had to enter the abdomen through polypropylene sutures, placed decades prior, and found the suture and original knot intact.

What is known is that all surgeries will initiate an inflammatory response, which is essential for healing, eventual tissue remodeling and scarring. As surgeons, we know this from medical school, from our residency training and our own surgical experiences. As graft material was developed first for abdominal hernia repair then used for sacrocolpopexy and finally introduced vaginally, the risks associated with each type, biological or synthetic, have been well described. A host response to a foreign body is well described and will include acute followed by chronic inflammation, granulation and encapsulation. With macroporous mesh, this occurs at the outside periphery of the fiber, and is snot systemic (Moalli, 2014).

Published reports attempting to evaluate or quantify the levels of inflammation have many inconsistencies and some of the techniques to preserve, transport and clean the various specimens may have contributed to abnormal findings if the mesh. Hill (2015) examined explanted slings but 43.8% had used various "conservative measures" and 31.6% had prior unsuccessful attempts at removal. The most common finding was mild inflammation and moderate fibrosis. They found that "Midurethral sling mesh excised for voiding dysfunction demonstrates elevated levels of inflammation compared to mesh that is excised for pain and/or exposure. The vaginal tissue fibrosis and giant cell reaction are similar in patients who undergo mesh excision for voiding dysfunction and pain, and/or mesh exposure." Mellano (2016) reported cultures from explanted sling through vaginal surgery. They only demonstrated low density bacterial colonization without any difference whether the mesh had been removed after a recent or chronic erosion or if the mesh was removed for voiding dysfunction or urinary tract infection with intact coverage. There was also no difference in culture comparing the contaminated exposed mesh when compared to a site of non-exposed mesh. This demonstrates possible vaginal contamination during the explanting surgery but also that despite having mesh exposure, in a contaminated environment, the mesh actually does not promote infection. Smith (2013) noted "relatively minimal inflammation", low rates of granulation (6.3%) and benign reactive changers with fibrosis in 70% of explants, fibrosis being a major component of any scar.

In a large retrospective cohort study, with matched controls, Chughtai (2017) demonstrated the absence of association between polypropylene mesh and systemic or autoimmune disease. They identified 2,102 patients having undergone polypropylene mesh augmentation pelvic prolapse repair and two matched control cohorts comprising 44,636 women undergoing colonoscopies and vaginal hysterectomy and followed them for over 6 years. There was no increased risk for the development of autoimmune disease after mesh based surgery.

As far as the carcinogenic properties of polypropylene, there has never been a causal effect documented (King, 2014). The one case of a clear cell carcinoma associated with chronic inflammation occurring near the site of a sub urethral sling mesh exposure, does not mean causation. Additionally, there is no reliable evidence that supports a causal connection of Polypropylene mesh including TVT-O to cancer. Prolene suture material has been FDA approved and utilized in many different surgeries in different areas of the body for over 50 years with high safety record. All over the world, in men and women, billions of sutures since the 1970's have been used in cardiovascular and ophthalmic surgery, neurosurgery, plastic and reconstructive surgery, as well as general, urological and gynecological surgery. Tens of millions of polypropylene hernia meshes have been inserted since the 1980's. Over three million suburethral sings and hundreds of thousands of apical and vaginal meshes have been used, without any evidence of systemic disease or associated cancer (King, 2014; Moalli, 2014; Linder, 2016; Adel 2016). The fact that the Oppenheimer effect was described in rats using various plastic disks in 1958, does not apply to humans and not in the filament or meshes that have been in use for decades. Millions of fibers of Prolene sutures have been in use since the 1960's, over 3 million women have had their incontinence cured by slings, millions of polypropylene meshes have been implanted for various hernia and prolapse surgeries around the world. If polypropylene was toxic or caused cancer, we would have seen evidence of this by now. The MSDS warnings, required by OSHA, of sarcoma formation and that polypropylene is not to be implanted in humans are statements meant for the manufacturers and handling of the raw materials. These statements are made due to liability concerns in the production of the final product (Moalli, 2014). An attempt to induce genomic instability after exposure failed (Webber). The Agency for Research on Cancer found no evidence of tumorigenicity of metallic or synthetic implants in humans.

The medical literature, along with clinical experience in residency, fellowship for some, and in actual practice, are the typical means by which surgeons get information about frequency and severity of complications. Through my training and experience, review of the medical literature, discussions with colleagues, experience with teaching procedures to others, and my review of FDA documents, society statements, and clinical guidelines, complications such as voiding dysfunction, incontinence or retention, recurrent urinary tract infections, dyspareunia, pain and scarring are well-known complications that can occur with any anti-incontinence surgery. We are taught this as early as medical school and it is discussed throughout surgical and gynecological residency. These complications are basic, elemental pelvic surgery risks and are not unique to TVT-O. Performing surgery is always a balance between risks and benefits and there are no risk-free surgeries. Even the most minor mundane procedure carries a risk of a significant adverse outcome. People have died as a result of a paper cut! The complications that are unique to the TVT-O transobturator surgery involve complications from the mesh (mesh erosion and exposure) and its surgical introduction, with knowledge that there is no overall statistical difference between the inside-out technique versus the outside-in. What cannot be accurately

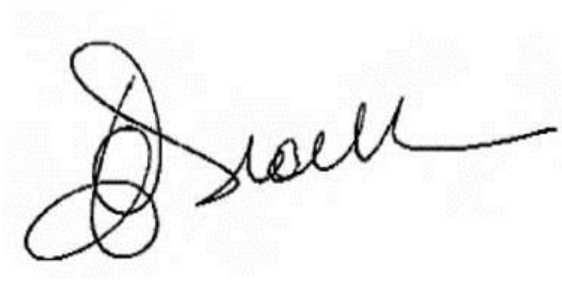
predicted is how a particular patient will react to a particular surgical procedure or implant; however, the vast body of literature has shown an impressive safety profile for TVT-O given the number of patients studied.

The PROLENE mesh used in TVT-O has a long track record of safety and efficacy over the last two decades. There is no evidence that any alleged degradation of the PROLENE mesh in the TVT-O causes any clinical effects over time. The appearance of foreign body reaction constitutes an anticipated reaction which is part of the inflammatory process necessary for integration of a foreign object into the surrounding tissue. There is no documented evidence that PROLENE mesh in itself causes infection, as the actual reports of infected mesh are rare. Despite the possibility of scarring,, the resulting size is still classified as an AMID Class I mesh with pores greater than 75 microns. TVT-O is commonly referred to as a large pore, lightweight mesh given its 1379 micron pore size (1.3 mm) and small surface area. TVT-O has one of the largest pore sizes out of the available midurethral slings, and its weight is comparable (Moalli 2008).

Table 1 Textile properties (including load at failure) provided by the manufacturers listed at the top (AMS, American Medical Systems) describing the different meshes tested in this study

Mesh type	Gynecare	Boston Scientific	AMS	Bard	Caldera	Mentor
Mesh thickness	0.63 mm	0.66 mm	0.66 mm	0.62 mm	0.48 mm	0.27 mm
Pore size	1379 µm	1182 µm	1000 µm	1160 µm	698 µm	374 µm
Fiber size (diameter)	0.15 mm	0.15 mm	0.15 mm	0.13 mm	0.15 mm	0.08 mm
Weight (g/m^2)	100	100	110	81	140	70
Relative porosity	53.9%	57.7%	52.1%	N/A	68.2%	N/A
Load at failure	70 N	70 N	65.6 N	60 N	70 N	76 N
Mesh edges/features	Tanged	Tanged/heat sealed midsection	Tanged/tensioning suture	Tanged	Not tanged	Not tanged; sealed edges

TVT-O has utility to surgeons because of its usability and reproducibility, significant improvements in objective and in subjective cures, quality of life. It has a low, acceptable and manageable complication risk profile, especially when compared to the traditional procedures. It is minimally invasive compared to laparotomy and utilizes mesh constructed of material which had been in use in the field for 50 years before it. TVT-O is reasonably safe for its intended use. There is no clinical evidence that demonstrates that TVT-O is defective.



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